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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/491,146	01/25/2000	Yury E. Khudyakov	03063-0381	8145

23859 7590 08/13/2003

NEEDLE & ROSENBERG, P.C.
SUITE 1000
999 PEACHTREE STREET
ATLANTA, GA 30309-3915

EXAMINER

LUCAS, ZACHARIAH

ART UNIT PAPER NUMBER

1648

DATE MAILED: 08/13/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/491,146

Applicant(s)

KHUDYAKOV ET AL.

Examiner

Zachariah Lucas

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 June 2003.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13, 16-19 and 31-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 17 and 19 is/are allowed.
- 6) ☒ Claim(s) 13, 16, 18, 31-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Status of the Claims

1. It is noted that, on page 3 of the Response filed by the Applicant on June 5, 2003, the Applicant identifies Claims 1-13, and 16-30 as pending in the Application, and claims 1-12, and claim 20-30 as withdrawn as to non-elected inventions. This is not an accurate statement. Claims 1-12, and 20-30 were cancelled from the Application in the Preliminary Amendment filed by the Applicant on January 25, 2003, paper number 6 of the Application file.

At present, Claims 13, 16-19, and newly added claims 31-34 are pending in the application. Claims 13, 16, and 18 were rejected, and claims 17 and 19 were objected to in the prior action, mailed December 3, 2002. Claims 13, 17, and 19 were amended, and claims 31-34 were added, in the Response filed June 5, 2003.

Claim Objections

2. **(Prior Objection- Withdrawn)** Claims 17 and 19 were objected to in the prior action for depending from rejected claims. These claims have been amended as independent claims. The objection is therefore withdrawn.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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4. **(Prior Rejection- Withdrawn)** Claims 13, 16, and 18 were rejected for lack of written description under 35 U.S.C. 112, first paragraph, as claiming nucleic acids encoding multiple epitope fusion proteins (a mosaic protein) “comprising more than two antigenic peptides from the same domain from different genotypes of hepatitis C virus,” although the application nowhere indicates that applicant considers the invention to include proteins wherein the epitopes from the same domain are not homologous to one another. In view of the amendment of the claims, this rejection is withdrawn.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. **(Prior Rejection- Withdrawn)** Claims 13, 16, and 18 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the amendment to these claims, the rejection is withdrawn.

7. **(New Rejection-Necessitated by Amendment)** Claims 31-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on mosaic proteins comprising “more than two homologous antigenic peptides from different genotypes of subtypes of a species...” However, the claim does not indicate what these

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genotypes or subtypes are a species of. It is suggested that the claim be amended to indicate that the peptides are from different genotypes or subtypes of hepatitis C virus.

Claim Rejections - 35 USC § 102

8. **(Prior Rejection- Withdrawn)** Claims 13 and 16 are rejected under 35 U.S.C. 102(a) as being anticipated by Yagi et al., Biol. Pharm. Bull., 19:1254-1260. In view of the amendment to the claims, and the arguments pursuant thereto, this rejection is withdrawn.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. **(Prior Rejection- Maintained)** The rejection of Claims 13, 16, and 18 under 35 U.S.C. 103(a) as being unpatentable over Khudyakov et al. (J. Virology 68:7067-7074) in view of Zhang et al. (J. Med. Vir., 45:50-55), Bukh et al. (Proc. Natl. Acad. Sci. USA, 91:8239-8243), and Chien et al. (Proc. Natl. Acad. Sci. USA, 89:10011-10015) was maintained in the prior action. Claim 13 describes a nucleic acid encoding a protein comprising more than two antigenic peptides from the same domain from different Hepatitis C genotypes. The Applicant traversed

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the rejection in the Response on five grounds. These grounds are: 1) The amendment of claim 13 avoids the prior art, 2) a prima facie case of obviousness has not been met, 3) There is not proper motivation to combine the teachings, 4) Chronological consideration of the art indicates an unsatisfied but long felt need in the art, and 5) The difficulties in the art teach away from a reasonable expectation of success. The second and third of these arguments each focus on the combination of Chien and Khudyakov to make a fusion protein of HCV viral epitopes. In view of this, these arguments will be considered together. These arguments are not found persuasive for the reasons indicated below.

The Amendment to claim 13 does not avoid the prior art.

First, the Applicant argues that the amendment of the claim such that the claims now read on embodiments wherein the fusion proteins comprise homologous antigenic peptides avoids the prior art. However, in view of the fact that Zhang teaches the use of multiple epitopes from homologous regions of the same protein, this traversal is not found persuasive. Because Zhang teaches the use of such homologous antigenic epitopes, it would have been obvious to those in the art to have used them in the fusion protein suggested by Khudyakov and Chien.

The teachings of Khudyakov and Chien are properly combined.

The Applicant's second and third arguments returns to the previous argument that the Examiner has not made a prima facie case of obviousness. In particular, the Applicant challenges the Examiner's conclusion that there is motivation to combine the Khudyakov and Chien references. The Applicant argues that the teachings of Khudyakov, which relate primarily to a fusion protein of HEV virus epitopes, does not support a suggestion for combination with the teachings of Chien to make an HCV fusion protein.

While the Applicant may be correct that the Examiner mistook the meaning of the last sentence of the Khudyakov abstract as referring to mosaic proteins generally, the teachings as a whole of Khudyakov still indicates that the teachings of that reference were intended to indicate that fusion proteins of other viral antigens be made. For example, on page 7073 of the reference, the authors specifically state that the results from tests with the HEV protein “strongly suggest that the HEV mosaic protein represents an innovative approach *that may have applicability to many other pathogens.*” (emphasis added). This statement, in view of the constant indications in the reference that the article is concerned with strategies for constructing such proteins, rather than a disclosure limited to HEV, provides adequate motivation to look to the combination of this reference with others teaching like proteins. See e.g., page 7072 (first paragraph under DISCUSSION, and right column), and page 7073 (left column, second paragraph). From this, it is no stretch to then assume that these other pathogens would include those of HCV, a pathogen referred to in the reference while discussing an alternative strategy of mosaic protein design, especially where the present reference indicates that the newer method has advantages over the other. See e.g., paragraph spanning pages 7072-7073. In view of the above, and for the reasons of record, this traversal is not found persuasive.

The Applicant has not established a long felt and unmet need for the Applicant's invention.

The Applicant has also argued that, if considered chronologically, the art references cited by the Examiner provide evidence of long felt need. The basis for this conclusion is apparently the fact that, after the Chien and Khudyakov references, Zhang indicates that those in the art had moved on to other methods by which the achieve the desired qualities. However, the

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development of other strategies alone is not sufficient to demonstrate an long felt and unmet need. For example, evidence that this development of alternative strategies stemmed from repeated failure of that suggested by the art would be indicative of the long felt and unmet need. Without such evidence, the Applicant has provided only naked argument without supporting evidence.

In this particular case, the Examiner also disagrees that Zhang demonstrates such a long felt need. In the prior action, the Examiner referred to a new reference, Yagi, which postdates Zhang, and indicates a continued interest in the mosaic protein model. While this reference does not specifically teach the protein currently claimed by the Applicant, it does indicate that the strategy described by Khudyakov had not been abandoned as unworkable by those in the art, and is therefore evidence that the long felt need has not gone entirely unmet until the Applicant's contribution. This traversal is therefore not found persuasive.

The Art does not teach away from a reasonable expectation of success.

The introduction of this section is somewhat deceptive. In the response to the Examiner's prior statements, the Applicant is no longer arguing that the art teaches away from the prior art. Instead, the Applicant takes issue with two statements by the Examiner in the prior action. First, the Applicant disagrees with the Examiner that, if he accepts the argument that the prior art does not provide a reasonable expectation of success, he would also have grounds to question the enablement of the Applicant for the broad scope of the claims. Second, the Applicant argues that, contrary to the Examiner's thoughts, the REAL method is not just a way to combine peptides.

These are related arguments in that the Applicant is arguing that, absent the use of the REAL method, making the claimed fusion protein based on the prior art would be unduly

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burdensome. However, while the Examiner agrees that the REAL method make simplify the process of making, and remaking the mosaic proteins such that operable embodiments may be found, the Examiner is not convinced that, if the problems in the art were so insurmountable, an easier method to combine peptides, and make and reform mosaic peptides would be sufficient to overcome the problems. In short, if the art of making these mosaic proteins was so unpredictable, the Applicant would need, in addition to a method of making the mosaic proteins, a method of identifying peptides that, when combined, would result in operative and useful chimeras. Thus, the Examiner does not agree with the Applicant that the making of mosaic proteins was beyond the art such that there was no reasonable expectation of success in making such proteins, and the REAL method used by the Applicant renders the mosaic protein obtainable, simply by facilitating the process of trial and error.

For the reasons above, and the reasons of record, the Examiner is not persuaded by the Applicant's traversal. The rejection is therefore maintained.

11. **(Prior Rejection- Maintained)** Claims 13, 16, and 18 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Valenzuela et al., U.S. Patent Number 6,428,792. The Applicant traverses this rejection on the grounds that Valenzuela does not teach all of the limitations of the presently claimed invention. The Examiner does not agree. Valenzuela teaches a fusion antigen comprising two or more copies of "equivalent antigenic determinant (for example, each copy is an epitope from a different viral strain)." Thus, the reference teaches a protein comprising multiple heterologous antigenic epitopes. While the

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reference teaches that there must be two or more, rather than at least three, such epitopes, these teachings are clearly overlapping.

The Examiner acknowledges that claim 13 of the present application does not correspond in scope to the protein taught by the present application. However, the distinction between the references is that, in addition to these at least two epitopes, the reference also requires the inclusion of other epitopes in addition to the at least 2. In view of the fact that the current claims read on mosaic proteins "comprising" more than three homologous epitopes, and because such language is open, and therefore inclusive of other additional epitopes, claim 13 encompasses the protein taught by the Valenzuela reference. Thus, the reference renders the currently claimed invention obvious. The Valenzuela reference teaches all of the limitations of the presently claimed proteins, although the Applicant does not teach all of the limitations of the Valenzuela proteins.

Conclusion

12. Claims 17 and 19 are found allowable.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after

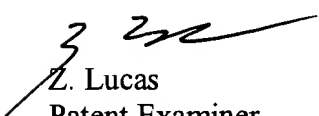
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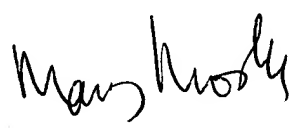
the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Z. Lucas
Patent Examiner
August 11, 2003


MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800
1600